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Acquired Immunodeficiency Syndrome in Children: Report of the Centers for Disease Control National Surveillance, 1982 to 1985

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ABSTRACT. Since national surveillance for acquired immunodeficiency syndrome (AIDS) began in 1981, the Centers for Disease Control (CDC) has received reports of more than 20,000 cases of AIDS in the United States. As of December 31, 1985, 307 of these cases had been diagnosed in children younger than 13 years of age. The number of cases is increasing rapidly. The number of cases reported in 1985 more than doubled those reported in 1984. The major risk factors in children for acquiring infection with the causative agent, human immunodeficiency virus (HIV), were (1) having a mother known to be infected and/or at increased risk for infection and (2) receiving a transfusion of blood or blood products. Of the 307 children with AIDS, 73% were reported from one of four states: New York, New Jersey, Florida, and California. Most AIDS cases in children occur in black or Hispanic infants and toddlers. The estimated incubation period for AIDS in children has increased each surveillance year, with the longest incubation exceeding 7 years. The prognosis for children with AIDS is poor and infants less than 1 year of age have the shortest survival time following diagnosis. Continued national surveillance for AIDS is mandatory for establishing effective prevention programs to control the spread of the disease. The CDC encourages all health care personnel to report cases of AIDS to their public health departments. *Pediatrics* 1987;79:1008-1014; *acquired immunodeficiency syndrome, epidemiology, immunosuppression.*

ABBREVIATIONS. AIDS, acquired immunodeficiency syndrome; CDC, Centers for Disease Control; HIV, human immunodeficiency virus.

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Since national surveillance for acquired immunodeficiency syndrome (AIDS) began in 1981, the Centers for Disease Control (CDC) has received reports of more than 20,000 AIDS cases in the United States. By the end of 1985, 307 of these cases had been diagnosed in children less than 13 years of age. Although they make up only 1% of the total number of AIDS patients, they have unique clinical, social, and public health problems that require special attention. These include issues related to pregnancy, fetal health, day care, foster care, school attendance, and immunizations.

Surveillance for AIDS in children has been an important tool in monitoring its incidence and epidemiology, in determining risk factors, and uncovering new modes of transmission of the causal agent, human immunodeficiency virus (HIV). In this paper, we report our analysis of cases of pediatric AIDS diagnosed through December 31, 1985, reported to the CDC.

METHODS

The surveillance system is based on practicing physicians and hospital personnel voluntarily reporting cases of pediatric AIDS to state or local health departments. AIDS is an officially notifiable disease in all 50 states, the District of Columbia, and Puerto Rico. Between September 1982 and September 1985, the CDC provided funding for surveillance to health departments in 17 states, six cities, and the territory of Puerto Rico. A standard case report form is used to assure uniform data collection.

The CDC case definition for AIDS in children is similar to that used for adult patients, namely,

unexplained cellular immunodeficiency as indicated by the presence of an opportunistic infection, Kaposi sarcoma, non-Hodgkins lymphoma, or primary lymphoma or the brain.^{1,2} The diseases that the CDC considers indicative of cellular immunodeficiency are listed in Fig 1. Pediatric cases are those occurring in children younger than 13 years of age.

In the summer of 1985, the CDC revised the original case definition for both children and adults to include less specific diseases that occurred in association with a positive test result for HIV infection (Fig 1).² For children, biopsy-proven chronic lymphoid interstitial pneumonitis is considered indicative of AIDS unless test results for HIV are negative.

The definition also requires that diseases that may mimic pediatric AIDS, such as congenital immune disorders and congenital infections, must be ruled out. Toxoplasmosis and congenital herpes simplex infection must be diagnosed after 1 month of age, and cytomegalovirus infection must be diagnosed after 6 months of age.

RESULTS

Temporal Trends

As in adults, the yearly incidence of AIDS in children has increased since the occurrence of the

Protozoal and Helminthic Infections
 Intestinal cryptosporidiosis causing chronic diarrhea
Pneumocystis carinii pneumonia
Strongyloides infection of the lungs, and CNS; dissemination infection
 Disseminated toxoplasmosis infection of internal organs other than liver, spleen, or lymph nodes
 Isosporiasis causing chronic diarrhea*
Fungal Infections
Candida esophagitis
 Bronchial or pulmonary candidiasis*
 Disseminated cryptococcosis or meningitis
 Disseminated histoplasmosis*
Bacterial Infections
 Disseminated atypical mycobacterial infections
Viral Infections
 Cytomegalovirus infection of internal organs other than liver, spleen, or lymph nodes
 Chronic mucocutaneous herpes simplex virus infection or infection of the lungs or gastrointestinal tract beyond the mouth, throat, or rectum
 Progressive multifocal leukoencephalopathy
Cancer
 Kaposi sarcoma
 Brain lymphoma
 Non-Hodgkin lymphoma*
Idiopathic Disease
 Chronic interstitial pneumonitis†

Fig 1. Diseases considered by the Centers for Disease Control to be predictive of underlying cellular immunodeficiency associated with AIDS. *Must also have a positive test result for human immunodeficiency virus (HIV). †Unless test results for HIV are negative.

earliest retrospectively diagnosed pediatric case in 1979. The first pediatric case was reported to the CDC in November 1982, about 18 months after the first case report in adults. The number of cases reported in 1985 is 2.7 times the number of cases reported in 1984 (Fig 2).

The time of transmission of the virus to children in whom AIDS developed can be estimated by year of birth for children who acquired the virus perinatally and by year of transfusion for those who acquired the virus through blood transfusion (Fig 3). The earliest year of birth for children with perinatally acquired AIDS is 1977. The earliest transfusion of blood that is known to have infected a child with HIV was given in 1978.

Risk Factors for Acquisition of HIV

Slightly more than three fourths of children with

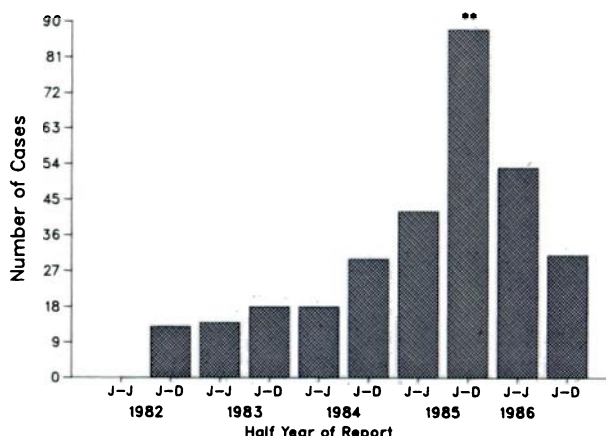


Fig 2. Pediatrics AIDS cases by date of report. Includes children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985. **Case definition changed to include chronic lymphoid interstitial pneumonitis.

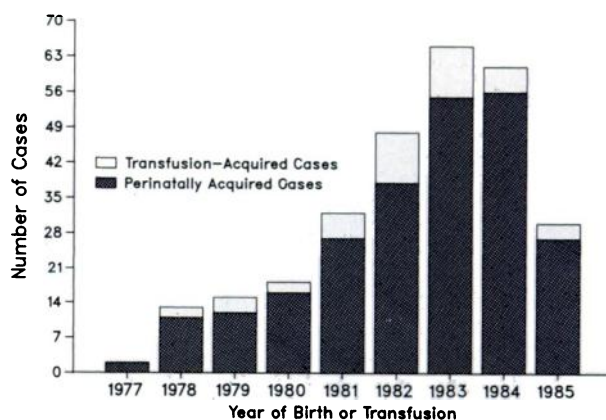


Fig 3. Pediatrics AIDS cases by year of transmission of human immunodeficiency virus. Includes children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985. Year of transmission was considered year of birth for perinatally acquired cases and year of transfusion for transfusion-acquired cases.

AIDS (n = 244) were born to mothers known to be infected with HIV or at increased risk for infection (Table 1). Of these 244 children, 74% (181) were born to mothers who were IV drug users or the sexual partners of IV drug users; 22% were born to mothers who became infected through heterosexual exposure to other infected men. For the latter group, this assumes that Haitian mothers who deny other risk factors such as IV drug abuse acquired HIV infection through heterosexual transmission, as studies among adults in this group have suggested.³⁻⁴

About one fifth of the children with AIDS had received one or more transfusions of blood or blood products (Table 1). The date of transfusion was known for 40 of the 44 nonhemophiliac children; all but two were transfused in the neonatal period.

At any given time, between 5% and 10% of pediatric cases cannot be classified in one of the established risk groups (see "no identified risk" category, Table 1), based on information in the initial case report form. That is, the mode of acquisition of HIV is unknown for these children. As these cases are reported, they are investigated by state and local health departments with the assistance of the CDC to determine whether these cases represent new modes of transmission of HIV. As information becomes available from these investigations, cases may be reclassified into the existing risk groups. Those in whom no further information can be obtained remain in the "no identified" risk category. If new modes of transmission are discovered through investigation of these cases, then new risk groups are created. Since the initiation of surveillance, 23 children were placed in the "no iden-

tified" risk category when initially reported. Through further investigation, 16 of these children were found to belong to an existing risk group and were reclassified; five children had died or their parents were lost to follow-up, and no further information was available; and two cases are still under investigation. The latter seven children remain in the "no identified" risk category (Table 1). None of these "no identified" risk investigations by the CDC and state and local health departments have provided evidence that these children acquired infection through casual contact in settings such as school, family, or day care. Furthermore, none of the reported pediatric AIDS cases were believed to result from either sexual abuse or IV drug use (either intentional or unintentional).

Geographic Distribution

The 307 pediatric cases reviewed here were reported from 23 states, the District of Columbia, and Puerto Rico; 73% of the cases were residents of one of four states: New York, New Jersey, California, and Florida (Fig 4). The proportion of patients with pediatric AIDS residing in these four states decreased in 1985 as compared with earlier years (Table 2). AIDS, particularly perinatally acquired disease, is primarily a disease of urban children, with 52% of the 307 patients residing in the standard metropolitan statistical areas of New York City, Newark, NJ, and Miami (Table 3).

The geographic distribution of the perinatally acquired cases differed from that of the transfusion-acquired cases. Of the 244 perinatally acquired cases, 75% were reported from New York, New Jersey, and Florida compared with 30% of the 44 transfusion-acquired cases.

TABLE 1. Risk Factors Associated With Pediatric AIDS Cases*

Risk Factor	No. (%) of Cases
Perinatally acquired	244 (79)
Mother	
IV drug user	148 (48)
Haitian born	43 (14)
Partner of IV drug user	33 (11)
Partner of bisexual man	9 (3)
Partner of infected man, risk unknown	1 (<1)
Partner of hemophiliac	1 (<1)
Received transfusion	1 (<1)
Infected, risk unknown	8 (3)
Transfusion acquired	44 (15)
Transfused in neonatal period	38 (11)
Transfused in childhood	2 (1)
Unknown data of transfusion	4 (1)
Hemophilia	12 (4)
No identified risk	7 (2)

* Includes children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985.

Opportunistic Diseases Associated With AIDS

Pneumocystis carinii pneumonia was the most

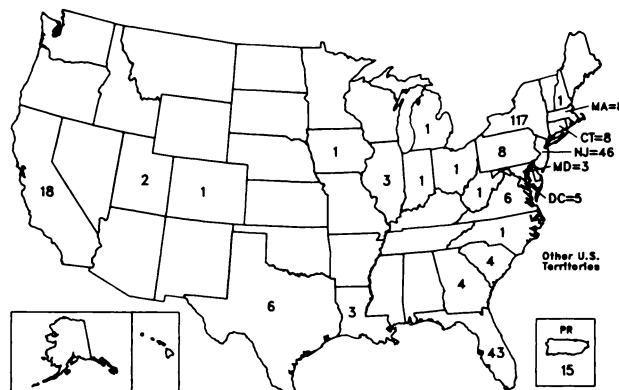


Fig 4. Pediatric AIDS cases by state of child's residence. Includes children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985.

TABLE 2. Reporting Trends for Pediatric AIDS in High and Low Prevalence Areas*

Year of Diagnosis	Proportion of Children With AIDS Residing in Area (%)		Total No. of Cases
	High Prevalence	Low Prevalence	
1979-1981	83	17	18
1982	78	22	23
1983	84	16	64
1984	78	22	78
1985	61	39	124

* Data from children less than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985. High prevalence areas include New York, New Jersey, Florida, and California; low prevalence areas include all other states.

TABLE 3. Incidence of Pediatric AIDS in Metropolitan Areas*

Year	New York		Newark		Miami	
	No.	Incidence	No.	Incidence	No.	Incidence
1979-1981	7	4.5	2	5.7	1	3.8
1982	8	5.2	1	2.8	3	11.5
1983	32	20.7	5	14.2	8	30.7
1984	33	21.3	5	14.2	5	19.2
1985	31	20.0	8	22.7	11	42.2
Cumulative	111	71.7	21	59.6	28	107.5

* Data from children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985. Incidence is the number of cases per 1,000,000 children younger than 13 years of age.

TABLE 4. Opportunistic Diseases and Malignancies Reported for Children With AIDS*

Disease	No. (%) of Diseases and Malignancies†
<i>Pneumocystis carinii</i> pneumonia	164 (53)
Lymphoid interstitial pneumonitis	156 (51)
Disseminated cytomegalovirus	57 (19)
<i>Candida</i> esophagitis	57 (19)
Disseminated <i>Mycobacterium avium</i>	23 (7)
Cryptosporidiosis	15 (5)
Chronic herpes simplex virus	15 (5)
Kaposi sarcoma	11 (4)
Cryptococcosis	4 (1)
Toxoplasmosis	2 (1)
Progressive multifocal leukoencephalopathy	1 (<1)

* Includes children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985.

† Some children had more than one disease present.

common opportunistic disease in the pediatric patients, occurring in 53% (Table 4). Kaposi sarcoma, a common malignancy in homosexual men with AIDS, was reported in only 11 children. All 11 were from the Miami area, and ten of the 11 cases were in children born of Haitian parents. Of the 307 children, 45% has other opportunistic diseases, of which lymphoid interstitial pneumonitis, *Candida*

esophagitis, and disseminated cytomegalovirus infection were the most common (Table 4). Fifty percent of the children had two or more opportunistic infections.

Age Distribution

In the pediatric population, AIDS is primarily a disease of infants and toddlers. Of the 307 cases, 80% ($n = 246$) were diagnosed in children younger than 3 years of age (Fig 5). Only 28 of the 307 children were of school age (5 to 13 years). Another 85 cases (not reviewed here) were reported in adolescents 13 to 19 years of age.

Estimated Incubation Period

Mean age at time of diagnosis of AIDS in children with perinatally acquired infection can be used to estimate the incubation period for AIDS. The mean age of all such children was 17 months (range 1 to 86 months). However, the mean age has increased over time ($P = .043$, linear regression analysis [Table 5]).

The incubation period may also be estimated by the time between transfusion of infected blood or blood products and the time of diagnosis of transfusion-acquired AIDS. Of the 40 transfusion-acquired cases in children (excluding children with hemophilia) with known dates of transfusion, the mean time between transfusion and diagnosis was 24.4 months (range 4 to 82 months). This incubation period was significantly greater than that observed for children with perinatally acquired AIDS ($P = .03$, t test).

Racial Distribution

Of the 306 patients with pediatric AIDS of known race, 178 (58%) were black, 71 (23%) were Hispanic, and 57 (19%) were white. The racial/ethnic distri-

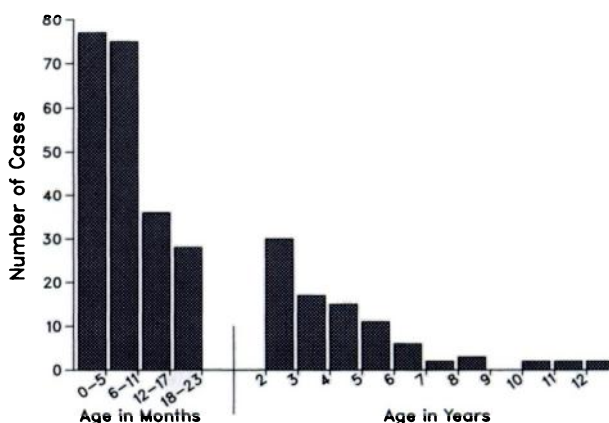


Fig 5. Pediatric AIDS cases by child's age at diagnosis. Includes children younger than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985.

TABLE 5. Trends in Estimated Incubation Period for Children With Perinatally Acquired and Transfusion-Acquired AIDS*

Year of Diagnosis	Perinatally Acquired				Transfusion Acquired			
	No. of Children	Mean (mo)	Median (mo)	Range (mo)	No. of Children	Mean (mo)	Median (mo)	Range (mo)
1981	9	8.0	5.0	3-20				
1982	14	17.3	14.0	3-44	4	15.3	12.0	10-27
1983	52	15.5	8.5	1-68	10	23.9	15.5	4-67
1984	66	16.8	9.0	1-79	9	23.3	15.0	8-68
1985	96	20.1	11.0	1-86	17	27.4	18.0	4-82
Cumulative	244	17.4	9.0	1-86	40	24.4	17.0	4-82

* Incubation period estimated from age at time of diagnosis for children with perinatally acquired AIDS and interval between transfusion and diagnosis for children with transfusion-acquired AIDS. Data from children less than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1985. Cumulative number of perinatally acquired cases includes seven cases diagnosed prior to 1981 and cumulative number of transfusion-acquired cases excludes four cases for whom the year of transfusion is unknown.

bution of children acquiring the virus from their mothers differed from that of children acquiring the virus from blood/blood product transfusion. Of the 244 children with perinatally acquired AIDS, 91% were black or Hispanic, compared with 43% of the 56 children with hemophilia or transfusion-acquired AIDS.

Sex Distribution

Overall, the sex distribution in children slightly favors boys, 53% compared with 47% girls. However, this distribution differs among risk groups. Of the perinatally acquired cases, 48% compared with 68% of the transfusion-acquired cases (excluding children with hemophilia) were in boys.

Prognosis

The proportion of children with AIDS who have died is high, and the median survival is less than 1 year. Overall, 68% of the 307 children were known to have died, and this proportion varied little among the risk groups. The reported children with AIDS survived a median of 9.4 months following diagnosis (standard error, 1.0 months), and 75% were dead by 23.7 months (standard error, 3.14 months). Survival time was not statistically different when analyzed by risk group, sex, or race (generalized Wilcoxon test [Breslow], generalized Savage test [Mantel-Cox]).

The proportion of deaths among infants (81%) (younger than 1 year of age) was significantly higher than the proportion of deaths among older children (55%) ($P < .001$, χ^2 test). The median survival time for infants (6.5 months, standard error 0.6 months) was significantly less than for older children (19.7 months, standard error 0.9 months) ($P = .001$, generalized Wilcoxon test; $P = .003$, generalized Savage test [Fig 6]).

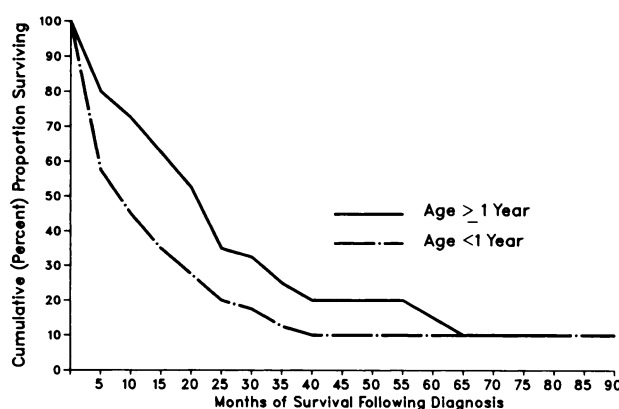


Fig 6. Survival time after diagnosis of AIDS in children less than 13 years of age in whom AIDS was diagnosed as of Dec 31, 1981, and reported to the Centers for Disease Control.

DISCUSSION

The number of children with AIDS reported to the CDC in 1985 has more than doubled the number reported in 1984. Even if we exclude those with only lymphoid interstitial pneumonitis to account for changes in the case definition, the number of cases reported in 1985 is 2.3 times that reported in 1984.

As the risk factors indicate, the two primary modes of transmission in children are perinatal exposure to infected mothers and transfusion of blood/blood products. The use of donor-screening programs⁵ and heat-treated coagulation products⁶ should virtually eliminate the latter form of transmission. The mean incubation period for children with transfusion-acquired AIDS is 24 months, and no transfusion-acquired cases were reported in children receiving blood after institution of donor-screening programs. However, a substantial number of children exposed to contaminated blood/blood products before the prevention recommendations remain at risk for AIDS.

The most common mode of HIV transmission in children is from infected mothers to their infants during the perinatal period. Little is known about perinatal transmission of HIV. Reports of AIDS in children who had no further contact with their mothers after birth^{7,8} and isolation of HIV from a 20-week fetus⁹ suggest that the virus can be transmitted in utero and/or at birth through exposure to infective maternal blood. One report of HIV infection in an infant who was breast-fed following a postpartum transfusion of HIV-infected blood in the mother¹⁰ and another report of isolation of virus from breast milk¹¹ suggest that transmission may occur through breast-feeding. The frequency of transmission from mothers to infants is unclear. It has ranged from 0% in a small group of infants born to mothers who were infected through artificial insemination¹² to 65% in various other groups who were studied.¹³⁻¹⁵

The geographic distribution of children with perinatally acquired AIDS parallels that of heterosexual adults with AIDS, 72% of whom reside in primarily urban areas of New York, New Jersey, and Florida. IV drug abuse or sexual contact with an IV drug user is reported by 69% of the heterosexual adult patients with AIDS. The prevalence of antibody to HIV in populations of IV drug users varies by geographic location with the highest rates in the New York City/Newark, NJ, areas (50% to 70%)^{16,17} and lower rates in Boston 42%,¹⁸ San Francisco 9%,¹⁷ and Chicago 11%.¹⁷ We can expect to see the number of pediatric cases increasing in other cities with large IV drug-using populations if transmission is not prevented in this population.

The Public Health Service has published recommendations for preventing perinatally acquired HIV infection.¹⁹ The recommendations stress that counseling services and testing for antibody to HIV should be offered to women at increased risk for infection. Infected women should be encouraged to postpone pregnancy until more is known about this mode of transmission. Uninfected women should be counseled to avoid infection. The Public Health Service has also published recommendations to reduce IV drug abuse-related and sexual transmission.²⁰

Based on the reported pediatric AIDS cases to date, the estimated incubation period of AIDS varies from 1 month to 7 years. The increase throughout time in mean age at diagnosis of AIDS indicates that the true mean incubation period may be longer than the mean period observed during these early years of the epidemic. A mathematical model of existing data for transfusion-acquired AIDS cases in adults predicted that the mean incubation period may be as long as 5 years.²¹

The racial/ethnic distribution of pediatric AIDS cases is related to the underlying risk factors for acquisition of infection. The preponderance of black and Hispanic children with perinatally acquired AIDS reflects the racial/ethnic composition of women at risk for HIV infection. Of the women with AIDS, 87% are black or Hispanic. The preponderance of white race among children with hemophilia and transfusion-acquired AIDS probably reflects the population of children receiving transfusions. The cumulative incidence rate for black children (27.4 cases per million population younger than 13 years) and Hispanic children (14.3) is 16 and eight times, respectively, the rate for whites.

The 1:1 male to female ratio observed among perinatally acquired cases indicates that boys and girls are equally susceptible to the infection by this route. However, a marked male preponderance was seen in the transfusion-acquired cases. This reflects, in part, the sex distribution of the transfused population of infants. Most (90%) of the children with transfusion-acquired AIDS were infants transfused in the neonatal period. A study of national trends in transfusion practice²² found that more male than female infants were transfused.

The prognosis for children with AIDS is poor; the proportion of deaths is high and survival time is short. The proportion of children reported here who are known to have died is probably an underestimate, because follow-up of patients who were alive at initial reporting varies from state to state, and not all deaths are reported. Survival analysis indicates that children in whom AIDS is diagnosed when less than 1 year of age have a more fulminant course compared with children in whom the diagnosis is made later in life. One study of 64 children with AIDS reported to the New York City Department of Health found that children with *P carinii* pneumonia had a more fulminant course characterized by diagnosis at an earlier age (mean age at diagnosis 11 months) than those with other opportunistic infections (mean age 31.4 months).²³ In the 307 children reported to the CDC, those younger than 1 year of age were more likely to have *P carinii* pneumonia (72%) compared with older children (38%) ($P < .001$, χ^2 test).

Because the CDC case definition requires the presence of an opportunistic disease, these statistics only reflect the more severe end of the spectrum of HIV infection. In one recent report, 14 (48%) of 29 symptomatic HIV-infected children met the CDC case definition for AIDS.²⁴

Because of the long incubation period of pediatric AIDS, cases reported at present represent transmission that occurred a mean of 1 to 2 years ago. By the time the first pediatric AIDS case had been

reported in November 1982, 45% of the children in whom the diagnosis was made by 1985 were already infected. Monitoring seroprevalence rates in mothers and children, particularly newborns, would give communities a head start in controlling HIV infection.

The national surveillance system has successfully monitored the occurrence of severe manifestations of HIV infection. It has been valuable in determining new modes of transmission and the frequency of different transmission routes and in assessing epidemiologic trends. Surveillance is vital for public health disease control and prevention. The CDC strongly encourages all health personnel to report AIDS cases to their local or state health departments.

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